J. Perinat. Med.
3 (1975) 47

The prediction of fetal lung maturity from the surface tension characteristics of amniotic fluid

E. Müller-Tyl, J. Lempert

1st University Clinic of Obstetrics and Gynecology (Chairman: Prof. Dr. E. GITSCH),
Experimental Division (Head: Prof. Dr. K. STEINBEREITHNER) of the Institute of Anesthesiology (Chairman: Prof. Dr. O. MAYRHOFER)
University of Vienna

Received April 5, 1974. Accepted June 18, 1974.

One of the basic characteristics of a mature infant lung is the presence of a surface active phospholipid-protein complex (surfactant) [2].

1 Introduction

The formation of surfactant commences in the second half of pregnancy and attains values for normal lung function between the 34th and 38th week [3, 16]. It is obvious from this relatively broad interval that the duration of pregnancy alone is of no predictive value for lung maturity.

During pregnancy surfactant is washed into the amniotic fluid from the lungs and can be demonstrated in the former [4, 9]. Lung maturity can be estimated from determinations of surfactant or its components. Both chemical and physical methods have been used [3, 5, 7, 11 12]. However, **most methods give a relatively high scatter of values and hence may be of limited significance.** We attempted to determine, whether surface characteristics of amniotic fluid would present more exact data concerning lung maturity. Our previous results [11] showed a continuous rise in surface activity of amniotic fluid during pregnancy. Hence it seemed worth while to examine more systematically a larger group of pregnancies. The relationship between the surface characteristics of amniotic fluid and the clinical data, i. e. lung maturity was also studied.

Curriculum vitae

ERICH MÜLLER-TYL *was born in 1941 in Vienna (Austria). He studied Medicine and obtained his M. D. degree in 1967. He then specialized in Obstetrics and Gynecology at the Empress Elizabeth Hospital in Vienna. Since 1971 he is at the 1st University Clinic for Obstetrics and Gynecology in Vienna.*

2 Material and methods

2.1 Normal values

To establish normal values during the second half of pregnancy for examination of amniotic fluid with a surface balance 98 amniotic fluid samples were collected by puncturing the amniotic sac. Only fluids from normal pregnancies that terminated with a full term infant with mature lungs were evaluated.

For the **surface balance** 12 ml amniotic fluid were placed into a specially made teflon trough. Surface tension was measured via a platinum plate connected to a force recorder while the surface was being rhythmically compressed and expanded from 100 to 20% of the initial area. Determinations were made at room temperature,

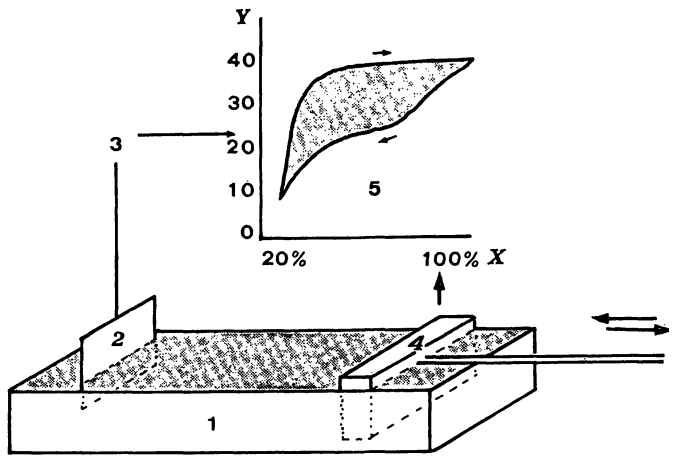

Fig. 1. Schematic representation of measurements with the surface balance. In the trough (1) we place amniotic fluid and the platinum plate (2) connected to a force recorder (3). Barrier (4) alters the surface area in a cyclic manner. The surface tension-area diagram (STD) is recorded with an X/Y recorder (5).

a cycle lasted 4 min. Surface tension and area were drawn with a x/y recorder in the form of a surface tension-area diagram (STD) (Fig. 1). The following parameters were evaluated: Surface tension at 100% area (y-max in dyn/cm) and at 20% of the area (y-min in dyn/cm) and the shape or hysteresis of STD.

2.2 Clinical experience

In 64 pregnancies that terminated 2 to 15 weeks prior to the calculated term, amniotic fluid was collected directly before or during delivery and was analysed on the surface balance. RDS was observed in 35 infants while no lung defect was noted in 29. RDS was diagnosed by the pediatrician using clinical and X-ray findings.

The material was divided as follows in relation to the clinical syndromes:

1. Died of RDS : 17 cases with a birth weight from 700 to 1700 g,
2. Survived with RDS: 15 cases with a birth weight from 1200 to 2600 g,
3. Infants with healthy lungs: 32 cases with a birth weight over 2000 g.

3 Results

3.1 Surface characteristics of amniotic fluid during pregnancy

Forty of the 98 samples were taken in the 40th week of pregnancy. The rest was collected between the 23rd and 40th week. During pregnancy there is a continuous rise in surface activity of amniotic fluid. Fig. 2 illustrates typical STD for the 23rd to 26th, 31st to 34th and 39th to 42nd week of pregnancy. In the 23rd week y-max is 55.7 $\pm$ 1.2 dyn/cm and y-min 36.3 $\pm$ 6.5 dyn/cm. These values decline to 47.8 $\pm$ 2.9 and 13.5 $\pm$ 4.6 dyn/cm respectively at term.

Fig. 3 summarizes surface tension parameters during normal pregnancy. It is obvious that **y-min is best suited for evaluating surface activity of amniotic fluid,** although this parameter does not show the largest age related changes. However, **it shows the smallest scatter of values.** Hence only y-min was used in the clinical application of our method.

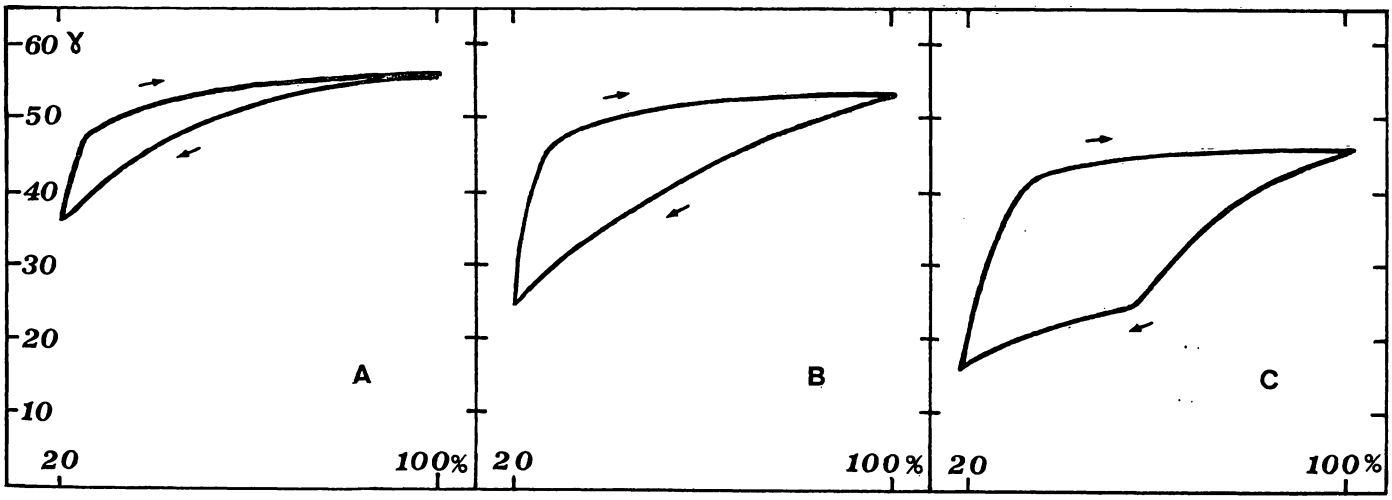

Fig. 2. Typical STD of amniotic fluid from weeks 23 to 26 (A), 31 to 34 (B) and 39 to 41 (C) of pregnancy.

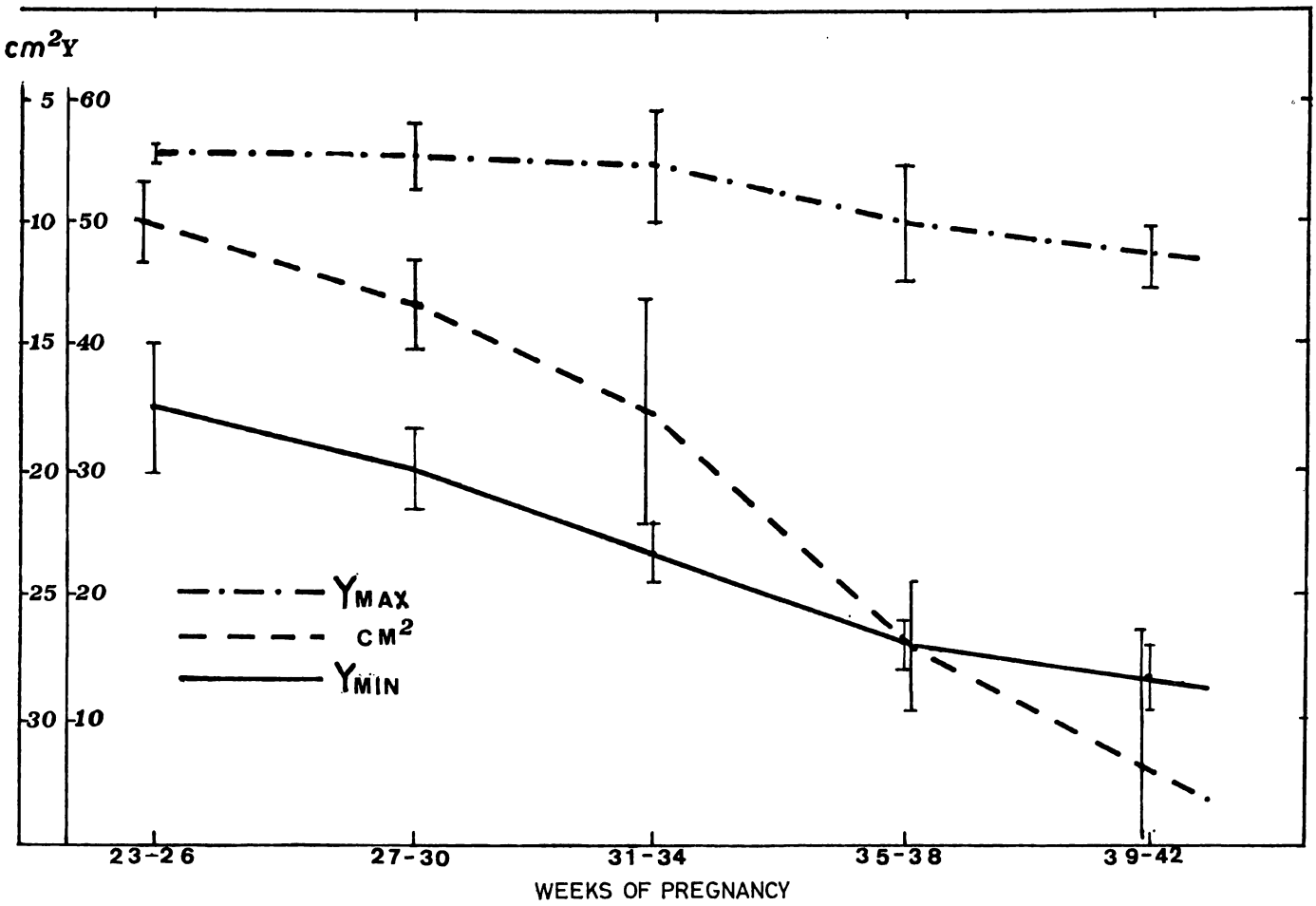

Fig. 3. Surface tension parameters of amniotic fluid during normal pregnancy. —·—·—· y-max (dyn/cm), - - - - hysteresis area (cm^2), ——— y-min (dyn/cm). Means ± S. D.

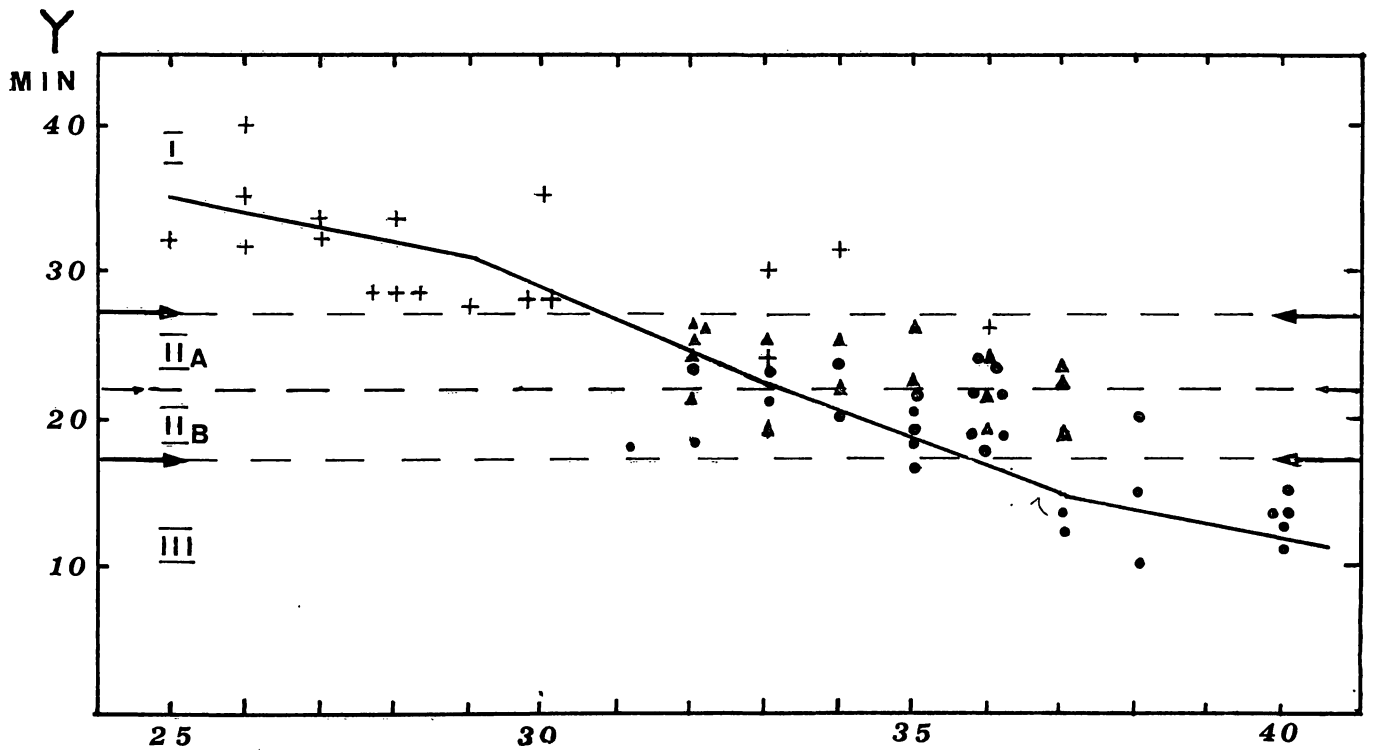

Fig. 4. y-min of amniotic fluid and clinical symptomatology of newborns. ○ healthy lungs, + died of RDS, △ survived with RDS. Relationship to gestational age. The curve for normal infants is also shown. Sector I: Lethal outcome, sector IIA: 70% chance for RDS, IIB: 30% chance for RDS, sector III: Healthy lungs.

3.2 Clinical use of the method for determining fetal lung maturity

An attempt was then made to establish a relationship between the clinical picture and y-min of amniotic fluid. Fig. 4 shows that a correlation between y-min values and the clinical picture results in **3 different sections.** The first (y-min 27 dyn/cm and up) contains 16 infants, all of whom died of RDS. In sector II (y-min between 27 and 17 dyn/cm) 2 infants died of RDS, 15 showed a transient respiratory insufficiency and 21 had healthy lungs. In sector III (y-min below 17 dyn/cm) there were 10 infants with healthy lungs. Since sector II contains all possible clinical states it seemed of advantage to subdivide it further:
In sector IIA (y-min 27 to 23 dyn/cm) 12 out of 17 infants had RDS while in IIB (y-min 22 to 17 dyn/cm) only 5 out of 17 infants showed this disease. It can thus be seen that as y-min decreases the probability of RDS occurrence also decreases.

4 Discussion

The rise in the concentration of surfactant components during pregnancy has been amply described [7, 9, 10, 12, 14]. A number of groups have used physical methods for surfactant demonstration in amniotic fluid. Agostoni [1] and Enhörning [6] published work on animal and human amniotic fluid. This work was not taken up since it had technical defects.
Clements [5] introduced a new method for surfactant demonstration in amniotic fluid. It is based on the property of surfactant to form foam after shaking with ethanol. The foam's stability depends on the maturity of the fetal lung, i. e. on the surfactant concentration. Although the simplicity of this method is attractive, indications of its unreliability have already been published [15].
Scarpelli [13] in 1967 was the first to use the surface balance to show extensive similarity between the surface characteristics of amniotic fluid at term and extracts from "mature" lungs of dead newborns. His results prompted us to examine the surface properties of amniotic fluid during pregnancy [11], with the aim of utilizing normal values for diagnosing fetal lung maturity.

A clinically useful method has to meet the following requirements:

1. Easy to perform and evaluate,
2. Not time consuming,
3. Reproducible results,
4. Small scatter of data.

Determinations made with the surface balance meet these requirements and hence make it possible to evaluate fairly accurately fetal lung maturity.
After obtaining normal values it was possible to utilize the method clinically. This seemed of particular importance since in recent years indications for the premature termination of pregnancy are more frequent than previously. This results in the more frequent occurrence of RDS. Inspite of some therapeutic progress [8] RDS is still a very serious illness in the newborn. **Since no really effective prophylaxis is known, the only alternative is to wait for the intrauterine maturation of the lungs.** Often, as shown by our results, only a short time interval is required to improve the chances of survival. Hence the reliability of the determination must be considered the decisive criterion for selecting a method for determining fetal lung maturity. Our method makes it possible to **differentiate three sectors on the basis of the y-min of amniotic fluid** and the clinical symptoms and hence to predict the post partum course and lung maturity of the infant. In sector I (y-min over 27 dyn/cm) lethal RDS must be expected. In sector III (y-min below 17 dyn/cm) the newborn should be without complications. For sector II (y-min 27 to 17 dyn/cm) a further subdivision seems to make predictions more exact. In sector IIA (27—23 dyn/cm) the probability of RDS occurring is 70% while in sector IIB (y-min 22 to 17 dyn/cm) the probability is only 30%.

5 Conclusion

Thus the determination of surface activity in amniotic fluid gives us a very reliable measure of lung maturity that is not dependent on the duration of pregnancy, which is often unreliable because of inaccurate term calculations.

Summary

In recent years fetal lung maturity has been assessed by chemical determination of lung surfactant components in the amniotic fluid. The variation in the results, however, limits the clinical usefulness of these methods. To establish reliable criteria for fetal lung maturity 98 specimens of amniotic fluid were obtained in the 23rd to 41st week of gestation and their surface properties measured in the **surface balance (Fig. 1).** A continuous rise in surface activity of amniotic fluid was observed during this period **(Fig. 2).** In the **evaluation of the surface activity of amniotic fluid y-min appears to be the most suitable parameter** because it shows a considerable change during the course of pregnancy and has **low variations (Fig. 3).** In 64 prematures amniotic fluid was obtained during delivery and its surface properties measured. The correlation of clinical symptoms of the premature with y-min of the amniotic fluid makes it possible to predict the fetal lung maturity at a given y-min-value **(Fig. 4).** When the results are arranged according to the incidence of RDS (lethal RDS, recovered from RDS and without RDS) **three y-min-ranges** can be clearly distinguished.When y-min of the amniotic fluid is over 27 dyn/cm the probability of lethal RDS is 100%, whereas when y-min is under 17 dyn/cm a mature lung can be expected. In the range between 27 to 17 dyn/cm any degree of lung maturity can be encountered. By division of this range in two additional ones a more accurate prediction of fetal lung maturity is possible: In the y-min-range 27—23 dyn/cm RDS-probability is approximately 70%, in the range 23—17 dyn/cm it is only 30% **(Fig. 4).** Measurements of surface activity of the amniotic fluid make it possible to predict fetal lung maturity and estimate RDS-probability.

Keywords: Amniotic fluid, fetus, lung maturity, surface tension.

Zusammenfassung

Zur Bestimmung der fetalen Lungenreife aus den Oberflächenspannungseigenschaften des Fruchtwassers

Obwohl seit einigen Jahren chemische Methoden zur Beurteilung der fetalen Lungenreife aus dem Fruchtwasser verwendet werden, ist die Aussagekraft der Ergebnisse dieser Methoden durch ihre Streubreite eingeschränkt. Um genauere Kriterien zur Lungenreifebestimmung zu erstellen, haben wir das Oberflächenspannungsverhalten des Fruchtwassers in der **Oberflächenwaage** untersucht **(Fig. 1).** Anhand von 98 Fruchtwasserproben aus der 23.—41. Schwangerschaftswoche konnte gezeigt werden, daß im Schwangerschaftsverlauf die Oberflächenaktivität des Fruchtwassers zunimmt **(Fig. 2). Von allen Oberflächenspannungsparametern hat sich y-min zur Beurteilung der Oberflächenaktivität des Fruchtwassers als besonders geeignet erwiesen.** Es erfährt im Schwangerschaftsverlauf eine starke Wertveränderung, weist aber nur eine **geringe Streubreite** auf **(Fig. 3).** Bei 64 Frühgeborenen wurde zum Zeitpunkt der Entbindung das Fruchtwasser gewonnen und dessen Oberflächenaktivität gemessen. Die Korrelation des klinischen Bildes der Frühgeborenen mit dem Oberflächenverhalten des Fruchtwassers ergab der jeweiligen Lungenreife entsprechende y-min-Werte **(Fig. 4).** Gliedert man die Ergebnisse nach dem klinischen Verlauf (an RDS verstorben, mit RDS überlebt und gesund), so lassen sich deutlich **drei Bereiche** erkennen: Im Bereich von y-min über 27 dyn/cm ist ein sicher letaler Verlauf zu erwarten, liegt y-min unterhalb 17 dyn/cm, so ist mit einem lungenreifen Neugeborenen zu rechnen. Im Bereich zwischen 27 und 17 dyn/cm traten sämtliche Verlaufsformen auf. Um die fetale Lungenreife genauer beurteilen zu können, haben wir in diesem Bereich eine weitere Teilung durchgeführt. Bei y-min-Werten von 27—23 dyn/cm liegt die Wahrscheinlichkeit des Auftretens von RDS bei etwa 70%, bei y-min-Werten zwischen 23 und 17 dyn/cm bei nur etwa 30% **(Fig. 4).** Untersuchungen der Oberflächenaktivität des Fruchtwassers ermöglichen eine Bestimmung der fetalen Lungenreife und somit eine Prognose über die Wahrscheinlichkeit des Auftretens eines RDS.

Schlüsselwörter: Fet, Fruchtwasser, Lungenreife, Oberflächenspannung.

Résumé

Prediction de la maturité pulmonaire foetale par l'etude de la tension superficielle du liquide amniotique

Ces dernières années, on a utilisé des méthodes chimiques de détermination des composants du surfactant pulmonaire dans le liquide amniotique pour évaluer la maturité pùlmonaire foetale. Les grandes variations observées dans les résultats, limitent cependant l'utilisation clinique de ces méthodes. Afin d'établir un critère de maturité pulmonaire foetale, nous avons pratiqué 98 prélèvements de liquide amniotique entre 22 et 40 semaines de grossesse, et nous avons évalué les propriétés de surface de chaque échantillon **(Fig. 1).** Pendant cette période, nous avons observé une augmentation permanente de ces propriétés **(Fig. 2). Parmi ces propriétés, la tension superficielle minimum constitue sans doute le paramètre le plus fidèle,** étant donné qu'elle se modifie de façon considérable au cours de la grossesse, et que sa mesure est reproductible **sans variations importantes (Fig. 3).** Nous avons mesuré la tension superficielle du liquide amniotique de 64 prématurés pendant l'accouchement. La relation existant entre les signes cliniques de prématurité et la tension superficielle minimum du liquide amniotique, rend possible la prédiction de la maturité pulmonaire foetale à partir d'une valeur de tension superficielle minimum donnée **(Fig. 4).** Lorsqu'on confronte les résultats avec l'incidence du syndrôme de détresse respiratoire (qu'il soit présent ou absent, mortel ou récupérable), on peut distinguer 3 valeurs de tension superficielle: lorsque

celle-ci est supérieure à 27 dyn/cm, il existe une probabilité de syndrôme de détresse respiratoire mortel de 100%. Au contraire, lorsque la tension superficielle est inférieure à 17 dyn/cm, on peut envisager l'existence d'une maturité pulmonaire suffisante. Entre 27 et 23 dyn/cm, la probabilité de l'existence d'un syndrôme de détresse respiratoire est de 70% environ; entre 17 et 23 dyn/cm, elle n'est que de 30% **(Fig. 4)**.

La mesure de la tension superficielle du liquide amniotique rend possible la prédiction de la maturité pulmonaire foetale, et l'estimation du risque de détresse respiratoire.

Mots-clés: Foetus, liquide amniotique, maturité pulmonaire, tension superficielle.

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Dr. E. Müller-Tyl
1st University Clinic of Obstetrics and Gynecology
Spitalgasse 23
A-1097 Wien IX/Austria